REMARKS

AMENDMENTS TO THE CLAIMS

With this amendment, claim 1 has been amended, the dependency of claim 20 has been changed to depend from claim 1 rather than withdrawn claim 19, and the dependency of claim 43 has been changed to depend from claim 1 instead of canceled claim 25. After entry of this amendment, the pending claim in this application will be claims 1-12, 16-18, 20-24, 26-28, 43, and 50, with claims 13-15 and 19 withdrawn as drawn to a non-elected species. The independent claims in this application are claim 1, from which claims 2-12, 16-18, 20-24, 26-28, and 43 depend or ultimately depend, and claim 50.

The following discussion addresses all of the Examiner's rejections in the Office Action under reply.

ENABLEMENT REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 stand rejected under 35 U.S.C. § 112, first paragraph, as nonenabling for the following: melanocortin peptides not disclosed in the specification; endothelin antagonists not disclosed in the specification; selective androgen receptor modulators not disclosed in the specification; neuropeptides not disclosed in the specification; and amino acids not disclosed in the specification.

This rejection is moot for canceled claims 25, 29, 31-39, 44-49, and 55 (the Examiner acknowledges the cancellation of claim 55 on page 1 of the Office Action) and is respectfully traversed for claim 50, which does not recite any of the secondary active agents identified by the Examiner. Although no longer relevant with the cancellation of claim 59, applicants note that claims 31-39 should not have been included in this rejection because they depended ultimately from claim 59 (claims 31-39 were dependent on claim 30, which was dependent on claim 59).

With respect to the remaining claims, applicants have amended independent claim 1 (from which claims 2-12, 16-18, and 20-29 depend) so that it sets forth exemplary melanocortin peptides, endothelin antagonists, selective androgen receptor modulators, neuropeptides, and amino acids as disclosed in the specification.

In light of the amendment to claim 1, the subject matter of claim 50, and the cancellation of claim 25, 29, 44, 45, and 55, applicants respectfully request reconsideration and withdrawal of this rejection for all pending claims.

WRITTEN DESCRIPTION REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description. This rejection is moot for canceled claims 25, 29, 44, 45, and 55 (again, claims 31-39 should not be part of this rejection because they ultimately depended from claim 59) and is respectfully traversed for the remaining claims.

For the remaining claims, the Examiner states at page 11 of the Office Action that there is no support in the specification for the cytokines of claim 1. Applicants respectfully direct the Examiner's attention to page 14, line 30 through page 15, line 6, where cytokines are disclosed as an example of peptidyl drugs that can be used for the treatment of female sexual dysfunction. At page 15, lines 1-6, examples of suitable cytokines that may be used within the context of the claimed invention are set forth. Because the specification provides an adequate written description for cytokines, applicants respectfully request reconsideration and withdrawal of this rejection for all pending claims.

OBVIOUSNESS REJECTION UNDER 35 U.S.C. § 103(a)

Claims 1-12, 16-18, 20-39, 43-45, 50, and 55-61 stand rejected under 35 U.S.C. § 103(a) as obvious over Adams (WO 99/66909) in view of Place et al (U.S. Patent No. 5,877,216), Othmer et al. (U.S. Patent No. 4,640,921), and Gioco et al. (U.S. Patent No. 5,565,466).

This rejection is moot for canceled claims 25, 29-39, 44, 45, and 55-61 and is respectfully traversed for the remaining claims.

The *prima facie* case is a procedural tool which, as used in patent examination, means not only that the evidence of the prior art would reasonably allow the conclusion the Examiner seeks, but also that the prior art compels such a conclusion if the applicant produces no evidence or argument to rebut it. *In re Spada,* 911 F.2d 705 (Fed. Cir. 1990). When establishing a *prima facie* case of obviousness, the Office must show that the cited prior art references, either singly or in combination, suggest the desirability of the claimed subject matter. *In re Deminski,* 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986). In particular, to establish a *prima facie* case of obviousness, three criteria must be met: first, the prior art reference must teach or suggest the claimed combination; second, the Office must show that the ordinary artisan would be motivated to modify the reference or to combine the reference teachings; and third, there must be a showing that the ordinary artisan would have a reasonable expectation of success at arriving at the claimed combination based *solely* on the teachings of the cited prior art reference. *In re Rouffet,* 149 F.3d 1350, 1357 (Fed. Cir. 1998); *In re Vaeck,* 947 F.2d 488 (Fed. Cir. 1991). If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more, the applicant is entitled to a grant of the patent. *In re Oetiker,* 977 F.2d 1443 (Fed. Cir. 1992).

As recited in independent claim 1, the present invention relates to a method for enhancing sexual desire and responsiveness in a female individual comprising orally administering to the individual *on an as-needed basis*, a therapeutically effective amount of an orally active androgenic agent as a first active agent and a therapeutically effective amount of a second active agent selected from rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, potassium channel blockers, and non-androgenic steroids.

Applicants note that claim 1 does *not* recite the following secondary active agents:

- vasodilating agents, which include prostaglandins and calcium channel blockers;
- dopamine agonists; or
- serotonin agonists.

As recited in independent claim 50, the present invention relates to a method for enhancing sexual desire and responsiveness in a female individual comprising orally administering to the individual on an as-needed basis, an orally active androgenic agent in an amount effective to provide a blood level of the agent or a metabolite thereof that approximates the blood level of the agent or a metabolite thereof during ovulation.

THE INVENTION AS CLAIMED IN CLAIM 1 ET SEQ.

Adams et al. teach the administration of apomorphine together with testosterone to induce a sexual response in female wistar rats. Adams et al. do not teach or suggest combining the testosterone with any other active agent other than apomorphine, which is a *dopamine agonist*. Specifically, Adams et al. do *not* teach or suggest combining testosterone with rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers. Accordingly, it follows that Adams et al. alone do not teach or suggest the invention as recited in claim 1 et seq.

Place et al. do not correct the deficiencies of Adams et al. Place et al. teach the administration of a *vasodilating agent*, such as a prostaglandin, together with a steroid or a steroid agonist, partial agonist, or antagonist, or an androgenic agent, such as testosterone or dihydrotestosterone, for the treatment of female sexual dysfunction (col. 8, ll. 28-53). Place et al. do not teach or suggest that the vasodilating agent and steroid or androgenic agent combination may include rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers. Accordingly, Place do not provide the missing teachings from Adams et al.

Othmer et al. do not correct the deficiencies of Adams et al. in view of Place et al. Othmer et al. teach the administration of buspirone, a *seroton agonist*, for the treatment of male or female sexual dysfunction. Othmer et al. do not teach or suggest combining the buspione with an androgenic agent or rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers. Accordingly, it follows that Othmer et al. do not provide the missing teachings from Adams et al. in view of Place et al.

Gioco et al. do not correct the deficiencies of Adams et al. in view of Place et al. and Othmer et al. Gioco et al. teach the administration of verapamil, *a calcium channel blocker*, for modulating male or female sexual responses. Gioco et al. do not teach of suggest combining the verapamil with an androgenic agent or rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers. Accordingly, it follows that Gioco et al. do not provide the missing teachings from Adams et al. in view of Place et al. and Othmer et al.

The foregoing discussion demonstrates that the hypothetical combination of Adams et al. in view of Place et al., Othmer et al., and Gioco et al. does not teach or suggest administering an androgenic agent together with rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers for enhancing female sexual response or desire. Further, the primary and secondary references each fail to provide any motivation for the ordinary artisan to modify the testosterone-apomorphine combination of Adams et al. such that the apomorphine is replaced with any one of rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers. Lastly, because the cited reference, alone or in combination do not mention that rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors, cytokines, selective androgen receptors modulators, neuropeptides, amino acids, serotonin antagonists, dopamine antagonists, potassium channel openers, or potassium channel blockers may be used for enhancing female sexual response or desire, it follows that the ordinary artisan could not have a reasonable expectation of success at arriving at the claimed invention solely by reading the cited references. Accordingly, it follows that the hypothetical combination of Adams et al. in view of Place et al., Othmer et al. and Gioco et al. does ***not*** render obvious the invention as it is recited in claim 1 et seq.

THE INVENTION AS CLAIMED IN CLAIM 50

Adams et al. teach that administering 480 μg/kg of testosterone to the female wistar rats at either the proestrus/estrus or metestrus/diestrus stages of the rat's estrus cycle increases the sexual response of the rats (pages 30-31, bridging para., and Fig. 5). In the discussion of the study, Adams et al. concentrate only on the levels of endogenous estrogen and progesterone that are in circulation during the different stages of the rat estrus cycle and do not mention the endogenous levels of testosterone that exist at any stage of the rat estrus cycle. Because Adams et al. do ***not*** teach or suggest that the 480 μg/kg of testosterone administered to the rats is an amount that approximates the blood level of the testosterone at any stage of the rat estrus cycle, it follows that Adams et al. are clearly not making a correlation between the administration of the 480 μg/kg of testosterone and the levels of endogenous testosterone during each stage of the rat estrus cycle.

Place et al. do not correct the deficiencies of Adams et al. The only reference to the administration of testosterone to a female individual in Place et al. is at col. 8, lines 28- 53 and claim 22. Within the discussion at col. 8 and at claim 22, no reference is made to the correlation between the administration of testosterone and the female individual's testosterone levels at ovulation. Accordingly, Place et al. do not provide the missing teachings from Adams et al.

Othmer et al. do not correct the deficiencies of Adams et al. in view of Place et al. Othmer et al. do not teach or suggest the administration of testosterone in concert with the buspirone disclosed therein for the treatment of female sexual dysfunction. Indeed, nowhere in Othmer et al. is testosterone even mentioned. Accordingly, it follows that Othmer et al. do not provide the missing teachings from Adams et al. in view of Place et al.

Gioco et al. do not correct the deficiencies of Adams et al. in view of Place et al. and Othmer et al. Like Othmer et al., Gioco et al. do not teach or suggest the administration of testosterone in concert with the verapamil disclosed therein for modulating male or female sexual responses. Indeed, nowhere in Gioco et al. is testosterone even mentioned. Accordingly, it follows that Gioco et al. do not provide the missing teachings from Adams et al. in view of Place et al. and Othmer et al.

The foregoing discussion demonstrates that the hypothetical combination of Adams et al. in view of Place et al., Othmer et al., and Gioco et al. does not teach or suggest administering an androgenic agent a for enhancing sexual desire and responsiveness in a female individual comprising orally administering to the individual on an as-needed basis, an orally active androgenic agent in an amount effective to provide a blood level of the agent or a metabolite thereof that approximates the blood level of the agent or a metabolite thereof during ovulation. Further, the primary and secondary references each fail to provide any motivation for the ordinary artisan to modify the testosterone-apomorphine combination of Adams et

al. such that the testosterone is administered in an amount that approximates the blood level of testosterone in the female wistar rats at ovulation. Lastly, because the cited reference do not teach or suggest administration of testosterone in an amount that approximates the blood level of testosterone of a female during ovulation, it follows that the ordinary artisan could not have a reasonable expectation of success at arriving at the claimed invention solely by reading the cited references. Accordingly, it follows that the hypothetical combination of Adams et al. in view of Place et al., Othmer et al., and Gioco et al. do ***not*** render obvious the invention as it is claimed in claim 50.

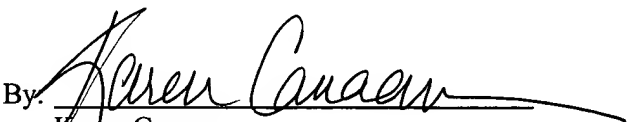
Because Adams et al. in view of Place et al., Othmer et al., and Gioco et al. do not render the claimed invention obvious, applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

As none of the cited references, alone or in combination, teach or suggest the claimed invention, it follows that applicants are entitled to a patent on the claimed subject matter. *See, In re Oetiker, supra.* Further, as applicants have addressed and resolved all of the Examiner's enablement and written description rejections, this application should now be in condition for allowance. Applicants, thus, respectfully request passage of this application to allowance.

Should the Examiner have any questions concerning this response, the Examiner is welcome to contact the undersigned attorney by telephone at 650-330-4913 or by e-mail at canaan@reedpatent.com.

Respectfully submitted,

By: 

Karen Canaan
Registration No. 42,382

REED & EBERLE LLP
800 Menlo Avenue, Suite 210
Menlo Park, California 94025
(650) 330-0900 Telephone
(650) 330-0980 Facsimile

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